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Indirubin, the active constituent of a Chinese antileukaemia medicine, inhibits cyclin-dependent kinases.

Hoessel R, Leclerc S, Endicott JA, Nobel ME, Lawrie A, Tunnah P, Leost M, Damiens E, Marie D, Marko D, Niederberger E, Tang W, Eisenbrand G, Meijer L.

Department of Chemistry, University of Kaiserslautern, Germany.

Abstract

Indirubin is the active ingredient of Danggui Longhui Wan, a mixture of plants that is used in traditional Chinese medicine to treat chronic diseases. Here we identify indirubin and its analogues as potent inhibitors of cyclin-dependent kinases (CDKs). The crystal structure of CDK2 in complex with indirubin derivatives shows that indirubin interacts with the kinase's ATP-binding site through van der Waals interactions and three hydrogen bonds. Indirubin-3'-monoxime inhibits the proliferation of a large range of cells, mainly through arresting the cells in the G2/M phase of the cell cycle. These results have implications for therapeutic optimization of indigoids.

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